EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Corlanor® (ivabradine tablets – Amgen)

TAC APPROVAL DATE: 05/06/2015

LAY CRITERIA EFFECTIVE DATE: 05/12/2015

OVERVIEW

Corlanor, a hyperpolarization-activated cyclic nucleotide-gated channel blocker, is indicated to reduce the risk of hospitalization for worsening heart failure (HF) in patients with stable, symptomatic chronic HF with left ventricular ejection fraction (LVEF) ≤ 35%, who are in sinus rhythm with a resting heart rate ≥ 70 beats per minute (bpm) and either are receiving maximally tolerated doses of beta blockers or have a contraindication to beta blocker use.[1] Corlanor is an inhibitor of the I_f current in the sinoatrial node, which slows heart rate (HR). The initial dose of Corlanor is 5 mg twice daily (BID). Following 2 weeks, assess the patient and consider dosage adjustment either upward (7.5 mg BID) or downward (2.5 mg BID) if needed to achieve a resting HR between 50 and 60 bpm. Thereafter, dosage adjustments can be made based on resting HR and tolerability. Corlanor should be taken with meals. The most common adverse events (AEs) were bradycardia (10.0%), hypertension (8.9%), and atrial fibrillation (8.3%). Bradycardia led to permanent withdrawal from the pivotal HF study in only 1% of patients given Corlanor. Also, approximately 2.8% of patients on Corlanor experienced luminous phenomena (phosphenes), which are thought to be caused by Corlanor's effects on retinal photoreceptors. Onset is usually within the first 2 months of therapy and most cases resolved during or after treatment. Corlanor has several contraindications including: use in patients with acute decompensated HF, blood pressure < 90/50 mmHg, sinus sick syndrome, sinoatrial block or third degree atrioventricular block, resting HR < 60 bpm, severe hepatic impairment and patients whose heart rate is maintained exclusively by the pacemaker. Corlanor is also contraindicated in patients receiving strong cytochrome P450 (CYP)3A4 inhibitors (e.g., azole antifungals, macrolide antibiotics).

Clinical Efficacy

The efficacy of Corlanor was established in one randomized, event-driven, multinational, double-blind, parallel-group pivotal trial called SHIFT (Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial) that compared Corlanor with placebo, in addition to standard HF therapies, in adult patients with stable New York Heart Association (NYHA) class II to IV HF, a reduced LVEF, and a resting HR of rate 70 bpm (n = 6,558).[1-2] The occurrence of the primary endpoint (a composite of the first occurrence of either hospitalization for HF or worsening HF or cardiovascular [CV] death) was reduced with Corlanor compared with placebo (hazard ratio 0.82; 95% confidence interval [CI]: 0.75, 0.90; P < 0.0001).

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Corlanor. All approvals are provided for 1 year in duration unless otherwise noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Corlanor is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Chronic Heart Failure (HF) in Patients Who Are Not Currently Receiving Corlanor.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   - **A)** The patient has a left ventricular ejection fraction (LVEF) ≤ 35%; AND
   - **B)** The patient is in sinus rhythm with a resting heart rate of ≥ 70 beats per minute (bpm); AND
   - **C)** The patient meets one of the following (i or ii):
     - **i.** The patient has tried or is currently receiving one beta blocker for heart failure treatment (e.g., metoprolol succinate sustained-release, carvedilol, bisoprolol, Coreg CR® [carvedilol extended-release capsules]); OR
     - **ii.** The patient has a contraindication to use of beta blocker therapy (e.g., bronchospastic disease such as chronic obstructive pulmonary disease [COPD] and asthma, severe hypotension or bradycardia).

   Corlanor is indicated to reduce the risk of hospitalization for worsening HF in patients with stable, symptomatic chronic HF with LVEF ≤ 35%, who are in sinus rhythm with a resting heart rate ≥ 70 bpm and either are receiving maximally tolerated doses of beta blockers or have a contraindication to beta blocker use.[1-2] In the SHIFT study, patients had NYHA class II to IV HF and were receiving other medications for HF, including beta-blockers (89%).[1-2] Beta-blocker therapy has many benefits in patients with heart failure (e.g., decreased mortality, HF hospitalizations, and death due to worsening HF) with metoprolol succinate sustained-release, carvedilol and bisoprolol having the best data.[3] However, use should be cautious in patients with bronchospastic disease (e.g., asthma), and some patients are unable to tolerate beta blocker therapy due to adverse events (e.g., fatigue, dizziness, hypotension, bradycardia).[3] In the SHIFT study, the primary reasons cited for the 11% of patients not receiving beta blockers at baseline were COPD, hypotension, and asthma.[1-2] The main reasons patients could not achieve the target beta blocker dose were hypotension, dizziness, a history of cardiac decompensation, and bradycardia.[1]

2. **Chronic Heart Failure in Patients Who Are Currently Receiving Corlanor.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** The patient had a left ventricular ejection fraction (LVEF) ≤ 35% prior to initiation of Corlanor therapy; AND
   - **B)** The patient meets one of the following (i or ii):
     - **i.** The patient has tried or is currently receiving one beta blocker for heart failure treatment (e.g., metoprolol succinate sustained release, carvedilol, bisoprolol, Coreg CR® [carvedilol extended-release capsules]); OR
     - **ii.** The patient has a contraindication to use of beta blocker therapy (e.g., bronchospastic disease such as COPD and asthma, severe hypotension).

   Corlanor is indicated to reduce the risk of hospitalization for worsening HF in patients with stable, symptomatic chronic HF with LVEF ≤ 35%, who are in sinus rhythm with a resting heart rate ≥ 70 bpm and either are receiving maximally tolerated doses of beta blockers or have a contraindication to beta blocker use.[1-2] Of note, Corlanor reduces the heart rate by approximately 10 bpm, which was sustained during the trial duration.[1] In the SHIFT study, patients had NYHA class II to IV HF and were receiving other medications for HF, including beta-blockers (89%).[1-2] Beta-blocker therapy has many benefits in patients with heart failure (e.g., decreased mortality, HF hospitalizations, and death

due to worsening HF) with metoprolol succinate sustained-release, carvedilol and bisoprolol having the best data.[3] However, use should be cautious in patients with bronchospastic disease (e.g., asthma), and some patients are unable to tolerate beta blocker therapy due to adverse events (e.g., fatigue, dizziness, hypotension, bradycardia).[3] In the SHIFT study, the primary reasons cited for the 11% of patients not receiving beta blockers at baseline were COPD, hypotension, and asthma.[1-2] The main reasons patients could not achieve the target beta blocker dose were hypotension, dizziness, a history of cardiac decompensation, and bradycardia.[1]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Corlanor has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Stable Angina Pectoris, in Patients Without Chronic Heart Failure.** Corlanor has been studied as a treatment for stable angina pectoris but further data are needed.[4-8] US guidelines addressing stable angina do not include Corlanor.[9-10]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date	Lay Criteria Effective Date
New Policy	Not applicable	05/06/2015	05/12/2015

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee.